Attorney Docket: 41577-344187

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
ALPAR ET AL.	Confirmation Number: **4547**
Serial No. **11/926,468**	Art Unit: **1645**
Filed: **October 29, 2007**	Examiner: **JaNa A. Hines**
For: **POLYCATIONIC CARBOHYDRATES AS IMMUNOSTIMULANTS IN VACCINES**	

DECLARATION OF PETER JAMES WATTS UNDER 37 C.F.R. §1.132

I, Peter James Watts, do hereby declare:

1. I am an expert in the fields of formulation science and drug delivery. I am currently Director, Pharmaceutical Development at Archimedes Development, Nottingham, UK, a licensee of the above-identified patent application. I hold degrees of Bachelor of Science in Pharmacy from Aston University, United Kingdom (1987) and Doctor of Philosophy in Pharmaceutics from Nottingham University, United Kingdom (1992). I consider myself an expert with respect to intranasal drug delivery compositions, including chitosan-containing compositions, and believe that others would also consider me to be such an expert. I have been named as an author on a number of papers reporting the use of chitosan in compositions for intranasal drug delivery. A full list of my publications is provided in Exhibit A.

2. I declare that the chemical term "chitosan glutamate" denotes a glutamate salt of chitosan.

3. I declare that trimethyl chitosan belongs to the class of compounds known as alkylated chitosan derivatives.

4. I declare that chitosan glutamate does not belong to the class of compounds known as alkylated chitosan derivatives or their salts. Chitosan and its salts, such as glutamate or hydrochloride, are chemically distinct entities from alkylated chitosan derivatives. Chitosan is a

weak base and salts are prepared by adding an acid, such as glutamic acid or hydrochloric acid. In this process, the glucosamine subunits ($R–NH_2$) (see Exhibit B, Fig 1A) of chitosan are converted to the soluble form ($R–NH_3^+$). This process is reversible in that adding a base will result in the glucosamine units losing their positive charge. Alkylated chitosan derivatives are prepared by covalently bonding alkyl groups to the glucosamine and/or N-acetyl glucosamine subunits of chitosan. For example, trimethyl chitosan may be prepared by methylation of the amino groups on chitosan (see Exhibit B, Fig 1B) using an agent such as methyl iodide. The resulting trimethylamino function provides trimethyl chitosan with an enhanced solubility profile compared to a chitosan salt; trimethyl chitosan remains soluble at higher pH values than a chitosan salt. For example, chitosan and its salts are insoluble above pH 6 whereas trimethyl chitosan remains soluble at pH 9.

5. I have read Example 3 and reviewed Figure 2 of U.S. Patent Application Serial No. 11/926,468. I declare that the experimental data presented in Figure 2 and discussed in Example 3 demonstrate that co-administration of trimethyl chitosans with a vaccine in experiments described in Example 3 produced an enhancement of the immune response in the experimental animals of groups 3 and 4 in comparison with co-administration of chitosan HCl with the vaccine in the experimental animals of group 2 or the experimental animals of group 1, which received the vaccines in conjunction with phosphate buffered saline. The immune response of group 2 appeared to be similar to that of group 1 indicating that chitosan HCl did not enhance the immune response in comparison with group 1.

6. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine, or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of any patent issuing on this application.

P J. Watts
Signature

P J. WATTS
Name

8 SEPTEMBER 2010
Date